

After the line beginning "Tadg15" and ending "DWIKENTGV~ ~~~~~ ~", please insert --(SEQ ID No: 2)--.

After the line beginning "Scce" and ending "R~~~~~ ~", please insert --(SEQ ID No: 4)--.

After the line beginning "Try" and ending "S~~~~~ ~", please insert --(SEQ ID No: 5)--.

After the line beginning "Chymb" and ending "PWVQKILAN ~~~~~ ~", please insert --(SEQ ID No: 6)--.

After the line beginning "Fac7" and ending "PRPGVLLRAP FP", please insert --(SEQ ID No: 7)--.

After the line beginning "Tpa" and ending "DWIRDNMRP~ ~~~~~ ~", please insert --(SEQ ID No: 8)--.

Please amend Figure 2 as follows:

After the line ending "R D W I K E N T G V", please insert --(SEQ ID No: 2)--

After the line "3121 TTCTTTTAAAAAAAAAAAAAAAAAAAA", insert --(SEQ ID No: 1)--.

Please amend Figure 3 by inserting --(SEQ ID No: 2)-- after the line "851 ENTGV".

Please amend Figure 11 as follows: In the line beginning "hTADG15 ENTGV\*" and ending "900", after "ENTGV\*", please insert --(SEQ ID No: 2)--.

In the line consisting of "mEpithin HP", after "HP" please insert --(SEQ ID No: 10)--.

Please amend Figure 12 as follows:

On the bottom of page 1, please replace FIGURE 12-1 with --Figure 12--

On page 2, after the line ending "3147", please insert --(SEQ ID No: 1)--.

On page 2, after the line ending "2900", please insert --(Seq ID No: 9)--.

On the bottom of page 2, please replace FIGURE 12-2 with --Figure 12 (continued)--

### **REMARKS**

#### **Objections to the Oath or Declaration**

A replacement Combined Declaration and Power of Attorney is enclosed herewith. The Applicants respectfully request that the objection to the oath or declaration be withdrawn.

### Objections to the Drawings

The drawings are objected to for various informalities. Figures 1, 2, 3, 11 and 12 have been amended herein. The changes to the figures are indicated in red on the enclosed copies and have only been made to introduce sequence identifiers into Figures 1, 2, 3, 11 and 12. Formal drawings will be submitted upon acceptance of the instant application.

### Objections to the Specification

The abstract has been objected to for not making reference to the claimed invention. This objection is respectfully traversed. The abstract has been amended to include the sentence --The instant invention also includes a kit containing antibodies for the detection of TADG-15 protein.-- Since, as amended, the abstract describes the instant invention, the Applicants respectfully request that the objection to the abstract be withdrawn.

The title has been objected to as not descriptive. This objection is respectfully traversed. The title has been amended herein. Therefore, the Applicants respectfully request that the objection to the title be withdrawn.

The disclosure has been objected to because the brief description of the figures lacks separate descriptions of Figures 12-1 and 12-2. This objection is respectfully traversed.

Figure 12 is improperly labeled as Figure 12-1 and 12-2. Figures 12-1 and 12-2 simply refer to the first and second pages of the same figure. Figure 12 has been amended herein to replace "Figure 12-1" with --Figure 12-- and "Figure 12-2" with --Figure 12 (continued)--. These changes are indicated in red on the enclosed copy of Figure 12. As such, the brief description of the figures is correct as is. Therefore, the applications respectfully request that this objection to the disclosure be withdrawn.

#### The 35 USC §112 Rejection

Claims 22-24 stand rejected under 35 USC §112, second paragraph, as indefinite. This rejection is respectfully traversed.

First of all, the Examiner states that the recitation "TADG-15" in claims 22 and 24 is vague and indefinite. Therefore, claims 22 and 24 have been amended herein to include the full name of the protein, i.e. Tumor Antigen Derived Gene-15. The Examiner also states that the recitations "fragment thereof" in claims 22 and 24 is vague and indefinite. Therefore, amendments

have been made herein to delete this recitation from claims 22 and 24. As amended, claims 22 and 24 are no longer vague and indefinite. Therefore, the Applicants respectfully request that the 35 USC §112, second paragraph, rejection of claims 22-24 as indefinite be withdrawn.

#### The 35 U.S.C. §103 Rejections

Claims 22-24 stand rejected under 35 U.S.C. §103(a), as unpatentable over GenBank Accession Number **W22987** (October 8, 1997), in view of **Lerner** (Nature 299:592-596, 1982). This rejection is respectfully traversed.

**W22987** describes the sequence of a serine protease expressed in the human colon carcinoma cell line COLO 201. This serine protease is identical to amino acids 615-855 of TADG-15. **Lerner** describes methods of generating antibodies of predetermined specificity to various antigens. The Examiner contends that it would be obvious to use the teachings of **Lerner** to generate an antibody against all or part of **W22987** to obtain an antibody against TADG-15 to incorporate into the kit of the instant invention. The Applicants respectfully disagree.

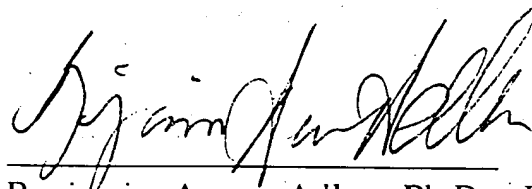
Claims 22 and 24 explicitly state that the antibody in the kit is "specific for TADG-15." An antibody raised against W22987 would not fit this criterion. Amino acids 615-815 correspond to the serine protease domain of TADG-15. As evidenced by Figure 1 of the instant specification, this domain is highly homologous to a number of other known serine proteases. Thus, this would not be the best segment to use to obtain an antibody specific for TADG-15. TADG-15 contains a number of domains which are not present in either W22987 or the other serine proteases of Figure 1. Therefore, given the knowledge that TADG-15 is 100% identical to another known protease starting after residue 615, it would be obvious that an antibody specific for TADG-15 must be generated from amino acid sequences before 615. Also, the Examiner seems to be implying that W22987 is a fragment of TADG-15. However, no evidence or suggestion that this is the case can be gleaned from the combination of W22987 and Lerner. Rather, W22987 presents the protein as a small, complete protease. However, even if it is a fragment of a larger protease, there is no suggestion that it is a fragment of TADG-15. Therefore, the applicant respectfully requests that the 35 U.S.C. §103(a) rejection of claims 22-24 under

as unpatentable over GenBank Accession Number **W22987** in view of **Lerner** be withdrawn.

This is intended to be a complete response to the Office Action mailed June 29, 2000. If any issues remain outstanding, the Examiner is respectfully requested to telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

Date: Sept 27, 2000



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DOCKET NO: D6064CIP

## COMBINED DECLARATION AND POWER OF ATTORNEY

Timothy J. O'Brien and Hirotoshi Tanimoto, as below-named inventors, hereby declare that: our residences, post office address and citizenship are as stated below next to our names; we believe we are the original, first and joint inventors of the subject matter which is claimed and for which a patent is sought on the invention entitled *TALG-15: An Extracellular Serine Protease Overexpressed in Carcinomas*, USSN 09/421,213 filed October 20, 1999.

We hereby state that we have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above. We acknowledge the duty to disclose all information we know to be material to patentability in accordance with Title 37, Code of Federal Regulations, §1.56(a), including information which became known to us between the filing date of the prior application and the national or PCT international filing date of this patent application.

We hereby appoint the following attorneys and/or agents to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: Dr. Martin L. McGregor, Registration No. 29.239 and Dr. Benjamin Adler, Registration No. 35.423. Address all telephone calls to telephone number 713/777-2321. Address all correspondence to, MCGREGOR & ADLER, 8011 Candle Lane, Houston, TX 77071.

We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

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New Address: Nakabu-cho 1-5-53-401, Marugame, Kagawa  
763-0033, JAPAN



\*

Heps	RIVGGRDTSL	GRWPQVSL.	....RYDG.A	HLCGGSLLSG	DWVLTAHCF	PE....RNRV	LSRWRFAGA	VAQASPHGLO
Tadg15	RVVGGTDADE	GEWPQVSL.	....HALGQG	HICGASLISP	NWLVSAHCF	IDDRGFRYS	PTQWTAFLGL	HDQSORSAPG
Scce	KIIDGAPCAR	GSHPWQVAL.	....LSGNQL	H.CGGVLVNE	RWVLTAHCF	.....K	MNEYTVHLGS	DTLG..DR.R
Try	KIVGGYNCEE	NSVPYQVSL.	....NSGYHF	..CGGSLINE	QWVVSAGHC.	.....Y	KSRIQVRLGE	HNIEVLEG.N
Chymb	RIVNGEDAVP	GSWPWQVSL.	....QDKTGF	HFCGGSLISE	DWVVTAAHC.	.....GV	RTSDVUVAGE	FDQGSDEELN
Fac7	RIVGGKVCBK	GECPWQVLL.	....LVNG.A	QLCGGTINT	IWVVSAAHCF	DKIKNWRNLI	....AVLGE	HDLSEHOGDE
Tpa	RIKGGLFADI	ASHPWQAIF	AKHRRSPGER	FLCGGILISS	CWILSAHCF	QERFPPHHL.	....TVILGR	.TYRVVPGEE

\*

Heps	LGVOAVVYHG	GYLPFRDPNS	EENSNDIALV	HLSS.PLPLT	EYIQPVCLPA	...AGQALVD	GKICTVTGWG	NTQYYGQQ.A
Tadg15	VQERRLKRII	SHPFNDFTF	D...YDIAL	ELEK.PAEYS	SMVRPICLPD	...ASHVFPA	GKAIWVTGWG	HTQYGGTG.A
Scce	AQRIKASKSF	RHPGYSTQT.	..HVNDMLV	KLNS.QARLS	SMVKKVRLPS	...RCE..PP	GTTCTVSGWG	TTTSPDVTFP
Try	EQFINAAKII	RHPQYDRKT.	..LNNDIMLI	KLSS.RAVIN	ARVSTISLPT	...APP..AT	GTKCLISGWG	NTASSGADYP
Chymb	IQVLKIAKVF	KNPKFSILT.	..VNNDITLL	KLAT.PARFS	QTVSAVCLPS	...ADDDFPA	GTLCATTGWG	KTKYNANKTP
Fac7	QSRRAQVII	P....STYVP	GTTNHDIALL	RLHQ.FVVL	DHVVPCLLPE	RTFSERTLAF	VRFSLVSGWG	QLLDGATAT
Tpa	EQKFEVEKYI	VHKEFDDDTY	D...NDIAL	QLKSDSSRCA	QESSVVRTVC	LPPADLQLPD	WTECELSGYG	KHEALSFFYS

\*

Heps	GVLQEARVPI	ISNDVONGAD	FYGN..QIKP	KMFCAGYPEG	G.....IDA	CQGDSSGGPFV	CEDSISRTFR	WRLCGIVSWG
Tadg15	LILQKGEIRV	INQTTCE..N	LLPQ..QITP	RMMCVGFLSG	G.....VDS	CQGDSSGGPL.	..SSVEADGR	IFQAGVVSWG
Scce	SDLKCVDKVL	ISPDQETKV.	.YKD..LLEN	SMLCAGIPDS	K.....KNA	CNGDSSGGPLV	C....R....	GTLOGLVSWG
Try	DELQCLDAPV	LSQAKCEAS.	.YPG..KITS	NMFCVGFLEG	G.....KDS	CQGDSSGGPVV	C....N....	GQLQGVVSWG
Chymb	DKLQQAALPL	LSNAECKKS.	.WGR..RITD	VMICAG..AS	G.....VSS	CMGDSSGGPLV	C....QKDG	WTLVGIVSWG
Fac7	ELMVLNVPR	MTQDCLQQR	KVGDSPNITE	YMFCAGYSDG	S.....KDS	CKGDSSGGP..	..HATHYRGT	WYLTGIVSWG
Tpa	ERLKEAHVRL	YFSSRCTSQH	LLNRT..VTD	NMLCAGDTRS	GGPQANLDA	CQGDSSGGPLV	CLN....DGR	MTLVGIISWG

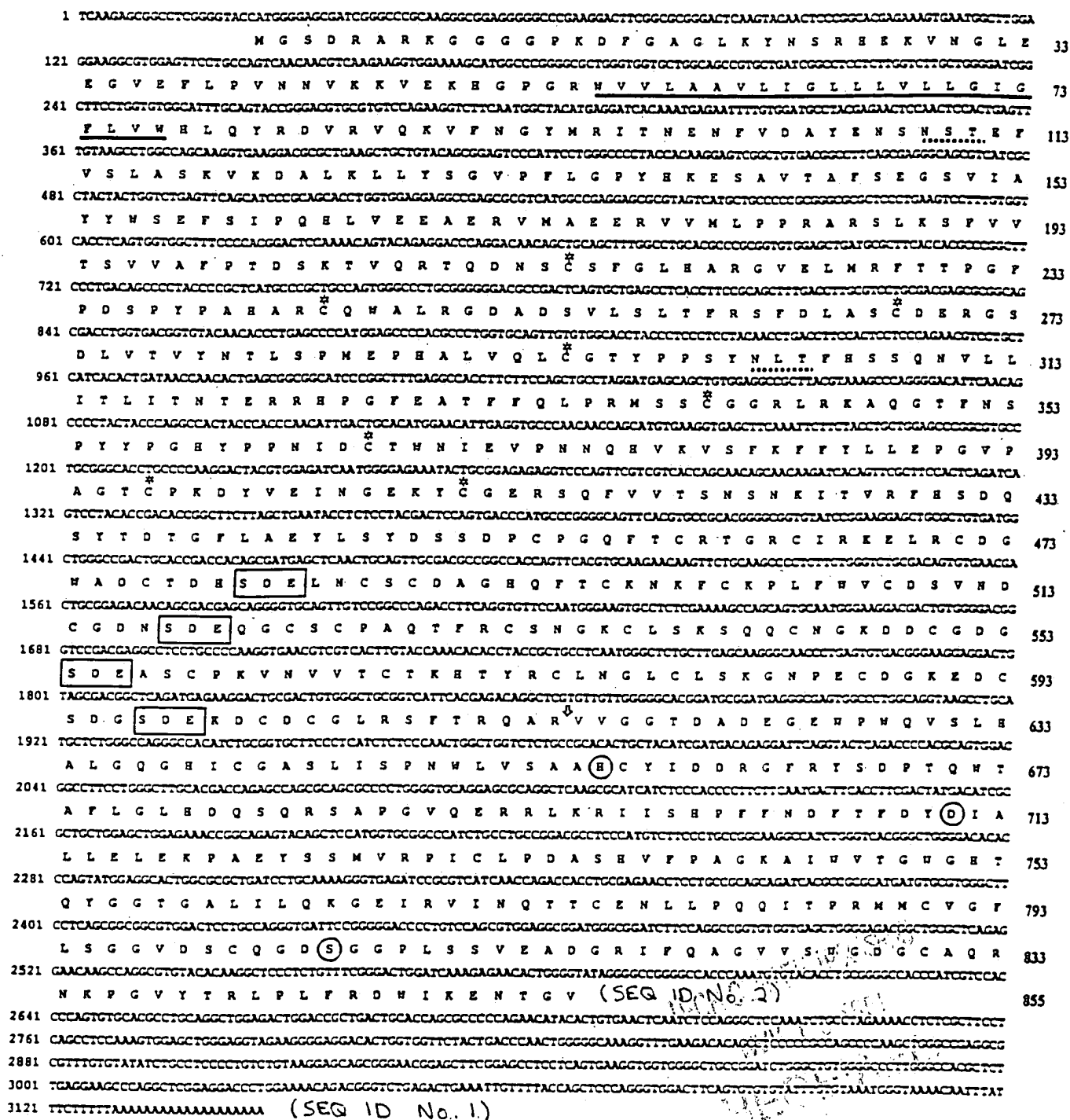
\*

Heps	T.GCALAQKP	GVYTKVSDFR	EWIFQAIKTH	SEASGMVTQL	-- (SEQ 10 No: 3)
Tadg15	D.GCAQRNKP	GVYTRLPLFR	DWIKENTGV-	-----	-- (SEQ 10 No: 2)
Scce	TFPCGQFNDP	GVYTQVCKFT	KWINDTMKKH	R-----	-- (SEQ 10 No: 4)
Try	D.GCAQKNKP	GVYTKVYNYV	KWIKNTIAAN	S-----	-- (SEQ 10 No: 5)
Chymb	SDTCS.TSSP	GVYARVTKLI	PWVQKILAA	N-----	-- (SEQ 10 No: 6)
Fac7	Q.GCATVGHF	GVYTRVSQYI	EWLQKLMRSE	PRPGVLLRAP	FP (SEQ 10 No: 7)
Tpa	.LGCGQKDVP	GVYTKVTNYL	DWIRDNMRP-	-----	-- (SEQ 10 No: 8)

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FIGURE 1



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1 MGSDRARKGG GPKDFGAGL KYNSRHEKVN GLEEGVEFLP VNNVKKVEKH  
51 GPGRWVVLAA VLIIGLLVLL GIGELVEHLQ YRDVRVQKVF NGYMRITNEN  
101 FVDAYENSNS TEEVSLASKV KDALKLLYSY VPFLGPYHKE SAVTAFSEGS  
151 VIAYYWSEFS IPQHLVEEAE RVMAEERVVM LPPRARSLSK FVVTSVVAFV  
201 TDSKTVORTQ DNSCSFGLHA RGVELMRETT PGFPDSPYPA HARÇQWALRG  
251 DADSVLSLTF RSFDLASÇDE \*RGSDLVTVYN TLSPEPHAL VQLCGTYPPS  
301 YNLTFHSSQN VLLITLITNT ERRHPGFEAT FFQLPRMSSC \*GGRLRKAQGT  
351 ENSPYYPGHI PPNIDÇTWN \*EVPNNQHVKV SFKFFYLLEP GVPAGTÇPKD  
401 YVEINGEKYÇ \*GERSQFVVTS NSNKITVRFH SDQSYTDTGF LAEYLSYDSS  
451 DPCPGQFTCR TGR CIRKELR CDGWADCTDH SDELNCSFDA GHQFTCKNKF  
501 CKPLFWVCD S VNDCGDN SDE QGCSCPAQTF RCSNGKCLSK SQÇNGKDDC  
551 GDG SDEASCP KVNVTCTKH TYRCLNGLCL SKGNPECDGK EDCSDC SDEK  
601 DCDCGLRSET ROARVVGTD ADEGEWPQV SLHALGQCHI CGASLSPNW  
651 LVSAH CYID DRGFRYSIPT QWTAFLGLHD QSORSAPGVQ ERRLKRIISH  
701 PFFNDFTFDY DIALLELEKP AEYSSMVRPI CLPDASHVFP AGKAIWVTGW  
751 GHTQYGGTGA LILQKGEIRV INQTTENLL PQQITPRMMC VGFLSGGVDS  
801 CQGS SGGPLS SVEADGRIFQ AGVVSWGDCG AQRNKPQVYT RLPLERDWIK  
851 ENTGV (SEQ ID No. 2)

1. Cytoplasmic domain
2. Transmembrane domain
3. CUB repeat
4. Ligand-binding repeat (class A motif) of LDL receptor like domain
5. Serine protease

: Conserved cysteine residue  
NEXT : Possible N-linked glycosylation site  
SDE : Conserved SDE motif  
Y : Potential cleavage site  
O : Conserved amino acids of catalytic triad II, D, S

FIGURE 3

htADG15 MGSLRARKGG GGPKDFGAGL KYNSRHEKVN GLEEGVEFLP VNNVKKVEKH 50  
mEpithin ---N-G--A- --SQ----- --D--L-NM- -F----- A--A-----R

htADG15 GPGRWVVLAA VLIGLLLVLL GIGFLVWHLQ YRDVRVQKVF NGYMRITNEN 100  
mEpithin --R-----V- --FSF--LS- MA-L----FH --N----- --HL-----I

htADG15 FVDAYENSNS TEFVSLASKV KDALKLLYSV VPFLGPYHKE SAVTAFSEGS 150  
mEpithin -L-----T- ---I---Q- -E-----NE --V-----K -----

htADG15 VIAYYWSEFS IPQHLVEEAE RVMAEERVVM LPPRARSLSK FVVTSVVAFP 200  
mEpithin ----- --P--A--VD -A--V----T -----A--- --L-----

htADG15 TDSKTVQRTQ DNSCSFGLHA RGVELMRFTT PGFPDSPYPA HARCQWALRG 250  
mEpithin I-PRML----- -----A--- H-AAVT----- ----N----- ----V---

htADG15 DADSVLSLTF RSFDLASCDE RGSDDLVTVYN TLSPMEPHAL VQLCGTYPPE 300  
mEpithin ----- ----V-P--- H-----D S-----V -R---FS--

htADG15 YNLTFHSSQN VLLITLITNT ERRHPGFEAT FFQLPRMSSC GGRLRKAQGT 350  
mEpithin -----L----- -F-V----- G---L----- ----K----- --V-SDT---

htADG15 FNSPYYPGHY PFNIDCTWNI EVENNQHVKV SFKFFYLLEP GVPAGTCPKD 400  
mEpithin -S----- ----N----- K---RN--- R--L---VD- N--V-S-T--

htADG15 YVEINGEKYC GERSQFVVT S NSNKITVRFH SDQSYTDTGF LAEYLSYDSS 450  
mEpithin -----GS -----S- --S---H- --H----- ----N

htADG15 DPCPGQFTCR TGR CIRKELR CDGWADCTDH SDELNCSCDA GHQFTCKNKE 500  
mEpithin -----M-M-K ----- ----P-Y ---RY-R-N- T-----Q-

htADG15 CKPLFWVCDS VND CGDNSDE QGCSCPAQTF RCSNGKCLSK SQQCNGKDDC 550  
mEpithin ----- ----G--- E-----GS- K-----PQ --K-----N-

htADG15 GDGSDEASCP KVNVTCTKH TYRCLNGLCL SKGNPECDGK EDCSDGSDEK 600  
mEpithin -----D S---S---Y ----Q----- ----T-----

htADG15 DCDCGLRSFT RQARVVGTD ADEGEWPWQV SLHALGQCHI CGASLISPNW 650  
mEpithin N----- K-----N -----L-----D-

htADG15 LVSAAHCIYID DRGFRYSPT QWTAFLGLHD QSQRSAPGVQ ERRLKRIISH 700  
mEpithin -----FQ- -KN-K---Y- M-----L- --K---S--- -LK-----T-

htADG15 PFFNDFTFDY DIALLELEKP AEYSSMVRPI CLPDASHVFP AGKAIWVTGW 750  
mEpithin -S----- ----S V---TV-----T-----

htADG15 GHTQYGGTGA LILQKGEIRV INQTTCEPLL PQQITPRMMC VGFLSGGVDS 800  
mEpithin ---KE----- ----D-M-----

htADG15 CQGDSSGGLS SVEADGRIFQ AGVVSWDGDC AQRNKPQVYT RLPLFRDWIK 850  
mEpithin ----- -A-K--M- -----E- -----CSSGLDQ

htADG15 ENTGV\* (SEQ ID No. 2) 900  
mEpithin RAHWGIAAWT DSRPQTPTGM PDMHTWIQER NTDDIYAVAS PPQHNPDCEL

htADG15 HP (SEQ ID No. 10) 902

FIGURE 11

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LOCUS       HSU20428      2900 bp      mRNA
DEFINITION  Human SNC19 mRNA sequence.
ACCESSION   U20428
NID         ql890631
KEYWORDS
SOURCE      human.
ORGANISM    Homo sapiens
            Eukaryota; Eukaryotes; Metazoa; Chordata;
            Vertebrata; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1 (bases 1 to 2900)
AUTHORS     Zheng,S., Cai,X., Geng,L., Cao,J., Jiang,L. and Zhi,Z.Z.
TITLE       SNC19 gene in Homo sapiens
JOURNAL     Unpublished
REFERENCE   2 (bases 1 to 2900)
AUTHORS     Zheng,S.
TITLE       Direct Submission
JOURNAL     Submitted (30-JAN-1995) Shu Zheng, Cancer Institute, Zhejiang
            Medical University, Hangzhou, 310009, Peoples Republic of China

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TADG15: TCAGAGCGGCCTCGGGGTACCATGGCGAATTTCGCTCCCTCCAGCTGGGAGGGTCCCCGAGGACTTTCGGCGCGGGACT 81

92 CAAAGTACAACTCCCGGCACGA-GAAGTGGAATGGCTTGGAGG--GGCGTAAATTTCCTGCTTAGTCA--AGTCA--G--GGTGG--AAGCATGGCCCCGGGG :91

182 CGCTGGGTGGTGGTGGCAGCCGGTCTGATCGGCCCTCTCTTGGTCTTCTTGGGATCGGGTTTCCCTGGTGGCATTTCAGTACCGGGACGTGCGGTGTC 281  
|||||  
1 CGCTGGGTGGTGGTGGCAGCCGGTCTGATCGGCCCTCTCTTGGTCTTCTTGGGATCGGGTTTCCCTGGTGGCATTTCAGTACCGGGACGTGCGGTGTC 100

282 ABAAGGCTCTTCAATGGCTACATGAGGATCACAAATGAGAATTTTGTGGATGGCTACGAGAACTCCAACTCCACTGAGTTTGTAAAGCCTGGCCAGCAAGGT 381  
101 ABAAGGCTCTTCAATGGCTACATGAGGATCACAAATGAGAATTTTGTGGATGGCTACGAGAACTCCAACTCCACTGAGTTTGTAAAGCCTGGCCAGCAAGGT 200

392 GATAGGACGCGCTGAGCTGCTGTACAGCGGAGTCCCATTCCTGGGGCCCTTATCAACAATGATGCTGCTGACCGCGCTTACGCGAGGGGACGCGTCATCGCC 481  
393 GATAGGACGCGCTGAGCTGCTGTACAGCGGAGTCCCATTCCTGGGGCCCTTATCAACAATGATGCTGCTGACCGCGCTTACGCGAGGGGACGCGTCATCGCC 482  
394 GATAGGACGCGCTGAGCTGCTGTACAGCGGAGTCCCATTCCTGGGGCCCTTATCAACAATGATGCTGCTGACCGCGCTTACGCGAGGGGACGCGTCATCGCC 483  
395 GATAGGACGCGCTGAGCTGCTGTACAGCGGAGTCCCATTCCTGGGGCCCTTATCAACAATGATGCTGCTGACCGCGCTTACGCGAGGGGACGCGTCATCGCC 484  
396 GATAGGACGCGCTGAGCTGCTGTACAGCGGAGTCCCATTCCTGGGGCCCTTATCAACAATGATGCTGCTGACCGCGCTTACGCGAGGGGACGCGTCATCGCC 485  
397 GATAGGACGCGCTGAGCTGCTGTACAGCGGAGTCCCATTCCTGGGGCCCTTATCAACAATGATGCTGCTGACCGCGCTTACGCGAGGGGACGCGTCATCGCC 486  
398 GATAGGACGCGCTGAGCTGCTGTACAGCGGAGTCCCATTCCTGGGGCCCTTATCAACAATGATGCTGCTGACCGCGCTTACGCGAGGGGACGCGTCATCGCC 487  
399 GATAGGACGCGCTGAGCTGCTGTACAGCGGAGTCCCATTCCTGGGGCCCTTATCAACAATGATGCTGCTGACCGCGCTTACGCGAGGGGACGCGTCATCGCC 488  
400 GATAGGACGCGCTGAGCTGCTGTACAGCGGAGTCCCATTCCTGGGGCCCTTATCAACAATGATGCTGCTGACCGCGCTTACGCGAGGGGACGCGTCATCGCC 489

492 TACTACTGGTCTGAGTTTACGATCCCCGACGACCTGGTGGAGGAGGCCCTTSCGCGTCTATGCGCCGATGAGCGCGTAGTCTATGCTGCCCGCCGCGGGCGCGCT 581  
301 TCTACTAGGACTGAGTTTACGATCCCCGACGACCTGGTGGAGGAGGCCCTTSCGCGTCTATGCGCCGATGAGCGCGTAGTCTATGCTGCCCGCCGCGGGCGCGCT 399

582 CCTCTGAAGTCCCTTTGTGGTCACTCTAGTGGTGGCTTTCCCCACGGACTCTTAAACAGTACAGAGGATCCAGGACACAGCTGCAGCTTTGGCCCTGCACGC 681  
|||||  
600 CCTCTGAAGTCCCTTTGTGGTCACTCTAGTGGTGGCTTTCCCCACGGACTCTTAAACAGTACAGAGGATCCAGGACACAGCTGCAGCTTTGGCCCTGCACGC 698  
|||||

692 CCACGGGTGTGGAGCTGATGCGCTTCACACGCCCGGGCTTCCCTGCACTTCTTACCTCCCTCATGCTCCCTGCCAGTGGCCCTGCCGGGGGACGCCGAC 781  
|||||  
693 CCGGGGTGTGGAGCTGATGCGCTTCACACGCCCGGGCTTCCCTGCACTTCTTACCTCCCTCATGCTCCCTGCCAGTGGCCCTGCCGGGGGACGCCGAC 532

[illegible]

577 GGAGCCCCCGCCCTGGTGCAGTTGTGTGGCAGCTACCCCTCCCTCCTAAGAGCTGAGCTTCCACT.CCTCCCA.GGACGTCCTGCTCATCACACTGATAA 974  
682 GGGAGCCCCCGCCCTGGTGCAGTTGTGTGGCAGCTACCCCTCCCTCCTAAGAGCTGAGCTTCCACTTCCCTCCCAAGGACGTCCTGCTCATCACACTGATAA 783

975 CCACACTGAGCGCGGCATCCCGGGCTTTGAGGCCACCTTCTTCCAGCTTCTTAGCATGAGCAGCTGTGTAGGCCCGCTTACGTAAAGCCAGGGGACATT 1074  
|||||  
984 CCACACTGAGCGCGGCATCCCGGGCTTTGAGGCCACCTTCTTCCAGCTTCTTAGCATGAGCAGCTGTGTAGGCCCGCTTACGTAAAGCCAGGGGACATT 881

1075 CACACAGCCCCCTACTACCCAGGCCACTACCCACCCAAACATTGACTGCACTGTCACACTTGGAGGTGCCCAACACCAGCATGTGTGAGGTGAGCTTCAATTC 1174

693 CACACAGCCCCCTACTACCCAGGCCACTACCCACCCAAACATTGACTGCACTGTCACACTTGGAGGTGCCCAACACCAGCATGTGTGAGGTGAGCTTCAATTC 981

1275 TTCTACCTGCTGGAGCCCCGGCTGCCTGCGGGGACCTGCCCCAGGATAGGTGAGATCATGSSGAGAAATACTCCGAGAGAGGCTCCAGTTCGTCTG 1274

982 TTCTACCTGCTGGAGCCCCGGGCTGCCTGCGGGACCTGCCCCAGGATAGGTGAGATCATGSSGAGAAATACTCCGAGAGAGGCTCCAGTTCGTCTG 1081

1275 TACCCAGCAACAGCAACAGATCAGAGTTCGGTTCCACTCAGATCAGTCTTACACCGACACCGGGTCTCTTAGCTGATACCTGTCTCTACGACTCCAGTGA 1374  
1092 TACCCAGCAACAGCAACAGATCAGAGTTCGGTTCCACTCAGATCAGTCTTACACCGACACCGGGTCTCTTAGCTGATACCTGTCTCTACGACTCCAGTGA 1181

1375 CCGATGCCCGGGGAGTTACGTGCCGCACGGGGCGGTGTATCCGGAAGAGCTCCGCTGTGATGCTGGGCCCACTGCACCGACCACAGCGATGAGCTC 1474  
1482 CCGATGCCCGGGGAGTTACGTGCCGCACGGGGCGGTGTATCCGGAAGAGCTCCGCTGTGATGCTGGGCCCACTGCACCGACCACAGCGATGAGCTC 1580

1475 AACCTGCAGTTGCGACCCGCCACCAGTTCACGTGCAAGACAGTATTTCAGGCCCTCTTCTGSGTCTGCGACAGTGTGACGACCTCCGGAGACACA 1574  
|||||  
1251 AACCTGCGTTCGCGACCCGCCACCAGTTCACGTGCAAGACAGTATTTCAG...CTCTTCTGSGTCTGCGACAGTGTGACGACGTGCGGAGACACA 1377

125) AAGTCCAGTTGCCAGCCCCGCCACGAGTTCAGGTGCAGAGCAAGTTCTTCAAG...CTCTTCTGGTCTGGCAAGTGTGAACGAGTGGGAGACAACT 1377

~~FIGURE 12-1~~ Figure 12